Kidney-ventilator interaction and kidney-protective ventilation

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Purpose of review
Invasive mechanical ventilation (IMV) is a cornerstone in the management of acute respiratory failure (ARF) and acute respiratory distress syndrome (ARDS); however, positive pressure ventilation (PPV) and injurious IMV can contribute to renal dysfunction. This review aims to summarize current evidence on kidney-ventilator interactions and explore strategies for kidney-protective ventilation.

Recent findings
The relationship between ARF/ARDS and acute kidney injury (AKI) is a major contributor to morbidity, mortality, and adverse outcomes among critically ill patients. PPV can induce hemodynamic and neurohormonal changes that may impair kidney function. Additionally, injurious IMV can exacerbate these effects and promote biotrauma, triggering inflammatory responses that further compromise kidney function. Conversely, AKI can exert both inflammatory and non-inflammatory effects, impairing pulmonary function. Lung-protective ventilation (LPV) using low tidal volume and conservative fluid management are strategies that may mitigate AKI. Extracorporeal organ support, including renal replacement therapy and extracorporeal membrane oxygenation, may facilitate LPV and be associated with improved outcomes in patients with IMV-associated AKI.

Summary
IMV influences lung-kidney interactions in a bidirectional manner. Evidence suggests the use of LPV, and extracorporeal organ support may mitigate dual organ injury. A thorough understanding of this interplay is essential to optimizing outcomes in critically ill patients receiving IMV.

Keywords
acute kidney injury, acute respiratory failure, lung–kidney interaction, mechanical ventilation, renal replacement therapy

INTRODUCTION

Critically ill patients often experience simultaneous organ dysfunction, with the lung and kidney forming a particularly vulnerable axis. The crosstalk between acute respiratory failure (ARF), including acute respiratory distress syndrome (ARDS), and acute kidney injury (AKI) is a major contributor to morbidity and adverse outcomes in critical illness. Invasive mechanical ventilation (IMV) is a cornerstone in the management of ARF/ARDS; however, positive pressure ventilation (PPV) and positive end-expiratory pressure (PEEP) have hemodynamic and neurohormonal effects that can adversely affect kidneys. Moreover, injurious IMV is recognized as a contributor to AKI. Conversely, AKI disrupts fluid, electrolyte, and acid-base balance, promotes systemic inflammation, and can negatively impact pulmonary function.

Lung-protective ventilation (LPV) in the management of ARF/ARDS may also confer kidney-protective effects. Additionally, optimized use of extracorporeal therapies – including renal replacement therapy (RRT), extracorporeal membrane oxygenation (ECMO), and extracorporeal CO_2 removal ($ECCO_2R$) – have emerged as strategies to support LPV in patients with both ARF/ARDS and AKI.

This review explores the epidemiology and mechanisms of kidney-ventilator interaction, highlighting current evidence on kidney-protective

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KEY POINTS

- The relationship between kidney and lung injury is bidirectional.
- Invasive mechanical ventilation (IMV), especially when injurious, can trigger early hemodynamic changes followed by neurohormonal activation and indirect inflammatory effects on the kidneys.
- Acute kidney injury (AKI) can cause both inflammatory and non-inflammatory damage to the lungs.
- Evidence suggests that lung-protective ventilation with low tidal volume and conservative fluid management may mitigate adverse renal effects and reduce the risk of AKI.
- Extracorporeal organ support represents a promising adjunctive strategy to support lung-protective ventilation and improve outcomes in patients with IMV-associated AKI.

ventilation strategies and the role of extracorporeal therapies in minimizing dual organ injury.

EPIDEMIOLOGY

Incidence of acute kidney injury in acute respiratory failure/including acute respiratory distress syndrome

ARDS is independently associated with 11-fold greater odds of developing AKI, with an incidence of 30–44% [1,2]. In the ARMA trial, 24% of ARDS patients developed AKI within 4 days of IMV [3]. This secondary insult dramatically increased mortality [4]. Patients with ARDS alone had a mortality of 28%, whereas those with both ARDS and AKI had a mortality of 58% [3]. The combination of ARDS and AKI also prolongs IMV duration and hospitalization compared to not having AKI [2]. Nearly half of these patients with ARDS received RRT [5].

Incidence of acute kidney injury during invasive mechanical ventilation

The incidence of AKI among patients receiving IMV for ARF/ARDS ranges from 25% to 60% [1]. IMV alone is associated with threefold greater odds of developing AKI [6]. This was consistent across various ventilator settings underscoring the intrinsic risk of IMV itself [6].

The relationship between IMV and AKI was particularly evident during the COVID-19 pandemic. Early in the pandemic, widespread use of IMV was accompanied by a high incidence of AKI treated with RRT [7]. The use of higher PEEP and conservative fluid management in this context likely portended higher risk [5]. A lower AKI incidence was later observed, particularly among older patients [8]. This trend coincided with a shift to broader use of high-flow oxygen therapy, further supporting a causal link between IMV and AKI [9].

AKI during IMV can further complicate the management of ARF. Evidence indicates that AKI frequently develops within the first 1–3 days after IMV initiation [10]. These patients experience higher mortality, longer durations of IMV, and extended ICU stays compared to those without AKI [10]. Conversely, AKI doubles the risk of developing ARF with approximately 75% of AKI patients receiving concurrent IMV [11–13]. The coexistence of IMV and AKI worsens clinical outcomes, with mortality increasing by four- to sixfold compared to either condition alone [13]. Oliguria is associated with longer IMV weaning, more ventilator-days, and longer ICU and hospital stays [14]. AKI present at the time of IMV initiation predicts prolonged ventilatory support and weaning [15]. Similar trends have been observed across various patient populations, with persistent AKI >7 days associated with prolonged IMV [16].

PATHOBIOLOGY OF LUNG–KIDNEY INTERACTION

In critically ill patients, ARF/ARDS can negatively impact kidney function through multiple mechanisms. Conversely, AKI can further impair lung function by disrupting acid-base, and fluid homeostasis and exacerbating systemic inflammation. These interactions reflect a bidirectional relationship between IMV and AKI.

Impact of invasive mechanical ventilation/ injurious invasive mechanical ventilation

Mechanistically, the complex interplay linking IMV to AKI involves hemodynamic alterations, neurohormonal dysregulation, and inflammatory pathways (Fig. 1).

Hemodynamic mechanisms

When employing higher PEEP or continuous positive airway pressure, renal hemodynamics can be negatively affected [17]. These effects are mediated by increased intrathoracic pressure, reduced venous return, elevated pulmonary vascular resistance, decreased cardiac preload, and reduced cardiac output (CO) [18]. This cascade can reduce renal blood flow (RBF), glomerular filtration rate (GFR), and urine

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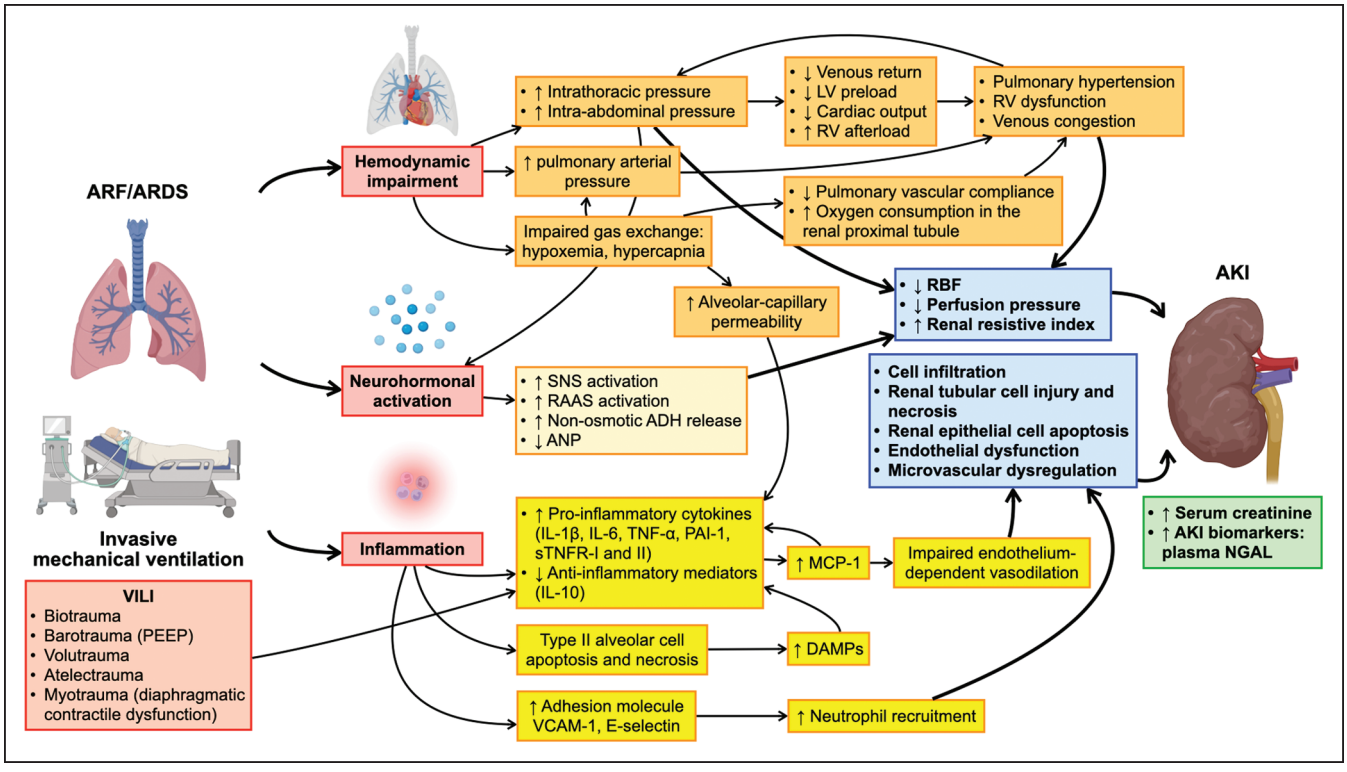

FIGURE 1. Invasive mechanical ventilation and acute kidney injury. Acute respiratory failure or acute respiratory distress syndrome increases the risk of acute kidney injury through multiple pathways, including hemodynamic alterations, neurohormonal activation, and inflammatory responses. Moreover, injurious invasive mechanical ventilation can induce ventilator-induced lung injury, which further amplifies the release of inflammatory cytokines, exacerbating renal dysfunction. ADH, antidiuretic hormone; AKI, acute kidney injury; ANP, atrial natriuretic peptide; ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; DAMPs, damage-associated molecular patterns; IL, interleukin; LV, left ventricular; MCP-1, monocyte chemoattractant protein-1; NGAL, neutrophil gelatinase-associated lipocalin; PAI-1, plasminogen activator inhibitor-1; PEEP, positive end-expiratory pressure; RAAS, renin-angiotensin-aldosterone system; RBF, renal blood flow; RV, right ventricular; SNS, sympathetic nervous system; sTNFR, soluble tumor necrosis factor receptor; TNF-α, tumor necrosis factor-α; VCAM-1, vascular cell adhesion molecule-1; VILI, ventilator-induced lung injury.

output [17]. Elevated central venous pressure can impair renal perfusion pressure, contributing to venous congestion and interstitial edema [19]. Morphologically, models of acute lung injury (ALI)-induced AKI found that rats ventilated with higher tidal volume (TV) have glomerular collapse, characterized by expansion of Bowman's space and collapse of capillaries, as well as perivascular edema [20].

Additionally, hypoxemia and hypercapnia can further compromise renal perfusion. Hypoxemia increases renal vascular resistance by activating vasoconstrictive mediators such as angiotensin II, endothelin, and norepinephrine, while suppressing vasodilators like nitric oxide [21]. These alterations not only reduce RBF but also contribute to pulmonary hypertension and right ventricular (RV) dysfunction, leading to acute cor pulmonale, which occurs in ~25% of ARDS patients [22]. This can worsen renal venous congestion, reduce oxygen delivery, and further impair GFR [23]. Hypercapnia induces renal vasoconstriction via norepinephrine release and increased oxygen consumption in the proximal tubules [24]. The combination of hypoxemia and hypercapnia can synergistically reduce RBF, resulting in ischemia and tubular apoptosis [25].

Neurohormonal pathways

IMV initiates neurohormonal cascades through elevated intrathoracic pressures that reduce atrial stretch and baroreceptor activation [26]. The decrease in right atrial filling pressure stimulates the sympathetic nervous system, activation of the renin-angiotensin-aldosterone system, and release of antidiuretic hormone (ADH), along with suppression of atrial natriuretic peptide (ANP) [27]. Animal studies involving cervical and carotid sinus denervation suggest that nonosmotic ADH secretion may be involved [28,29]. Clinical studies still debate whether ANP suppression

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directly impacts GFR [26,30]. Collectively, the net effect of these responses is sodium and water retention, reduction in RBF and GFR through, and the development of oliguric AKI [27].

Inflammatory crosstalk

Injurious IMV can provoke systemic inflammatory crosstalk, directly contributing to de novo or exacerbating existing AKI. A pivotal trial in ARDS patients found that those receiving conventional TV exhibited higher levels of systemic and intrapulmonary cytokines – including tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, IL-6, IL-8, and soluble TNF receptors (sTNFR) – compared to patients managed with a low TV strategy [31]. These cytokines promoted renal tubular epithelial cell (RTEC) apoptosis, endothelial dysfunction via Fas-ligand dysregulation, and increased vascular permeability through vascular endothelial growth factor (VEGF) [32].

Higher TV and airway pressures disrupt the alveolar-capillary barrier, leading to alveolar overdistension and mechanical injury, also known as ventilator-induced lung injury (VILI) – including biotrauma, volutrauma, barotrauma, atelectrauma, and myotrauma [33]. VILI can trigger the release of pro-inflammatory cytokines and damage-associated molecular patterns (DAMPs) into the systemic circulation [33,34]. In preclinical models, high TV ventilation (20 ml/kg) has been shown to elevate IL-6 levels in kidney tissue, upregulate AKI biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), and cause histologic evidence of tubular injury [31,32,35]. These effects are mediated by circulating inflammatory mediators, including plasminogen activator inhibitor-1 (PAI-1), VEGF, adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1) and E-selectin, and DAMPs such as extracellular nicotinamide phosphoribosyl transferase (NAMPT), which activate the toll-like receptor 4/nuclear factor-κB (TLR4/NF-κB) signaling pathways [36–38]. These factors contribute to endothelial dysfunction, microvascular injury, and increased vascular permeability within kidneys [3,39].

Impact of acute kidney injury on respiratory mechanics

AKI can significantly impact pulmonary function, particularly in patients receiving IMV. The accumulation of uremic toxins, fluid overload, and metabolic acidosis can negatively affect lung mechanics and gas exchange [40] (Fig. 2). These effects are associated with higher plateau pressure, lower lung compliance, elevated driving pressure, and lower PaO_2/FiO_2 [10]. Conservative fluid strategies can improve lung mechanics and reduce IMV duration [41].

Interestingly, these deleterious effects on lung function persist even in individuals with a net negative fluid balance, indicating that the pathophysiology is not solely attributable to hydrostatic pulmonary edema and may be resistant to RRT [42]. Experimental models of ischemia-reperfusion injury-induced AKI have shown disrupted alveolar-capillary integrity through systemic inflammation, oxidative stress, and impaired clearance of inflammatory mediators [42]. These mechanisms include the accumulation of indoxyl sulfate in lung tissue and downregulation of epithelial sodium channels (ENaC), Na^+/K^+-ATPase, and aquaporin-5 (AQP-5), which are critical for alveolar fluid clearance [43]. These changes contribute to pulmonary vascular congestion, alveolar hemorrhage, and interstitial edema – even in the absence of volume overload – highlighting the presence of diuretic-resistant, non-hydrostatic (nephrogenic) pulmonary edema [42]. Furthermore, this model has also demonstrated apoptosis of pulmonary epithelial cells [44].

Additionally, the pulmonary impact of AKI is driven by a complex cascade of inflammatory mediators [45]. AKI initiates the release of cytokines, DAMPs, and immune-modulating molecules into the circulation [45]. These bind to receptors on pulmonary cells, triggering inflammation, increased vascular permeability, and noncardiogenic pulmonary edema [46]. Elevated IL-6 levels correlate with prolongation of IMV and increased mortality [47]. Other key mediators released from injured kidneys include IL-8, TNF-α, high-mobility group box-1 (HMGB1; which signals via TLR4), mitochondrial deoxyribonucleic acid, and osteopontin [48–55]. Experimental studies have shown that necrotic slurry from damaged RTECs also increases cytokine and adhesion molecule production in pulmonary endothelial cells, enhancing vascular permeability and inflammation – reinforcing the role of the kidney as a source of pro-inflammatory signals that affect the lungs following AKI [56].

A recent study identified a mechanism of AKI-induced lung inflammation and hypoxemia driven by intravascular neutrophil retention within alveolar capillaries – also called neutrophil trains – which reduce pulmonary capillary blood flow. This phenomenon depends on the neutrophil chemoattractant CXCL2, released by activated classical $CCR2^+$ monocytes [57▪▪]. This finding implies that in direct ALI, neutrophils are abundant within the alveolar space, whereas in indirect insults such as AKI, they are typically absent. This supports the notion that many pulmonary complications during AKI are independent of volume overload. Volume removal alone will not completely resolve hypoxemia in most patients with AKI, and excessive volume removal

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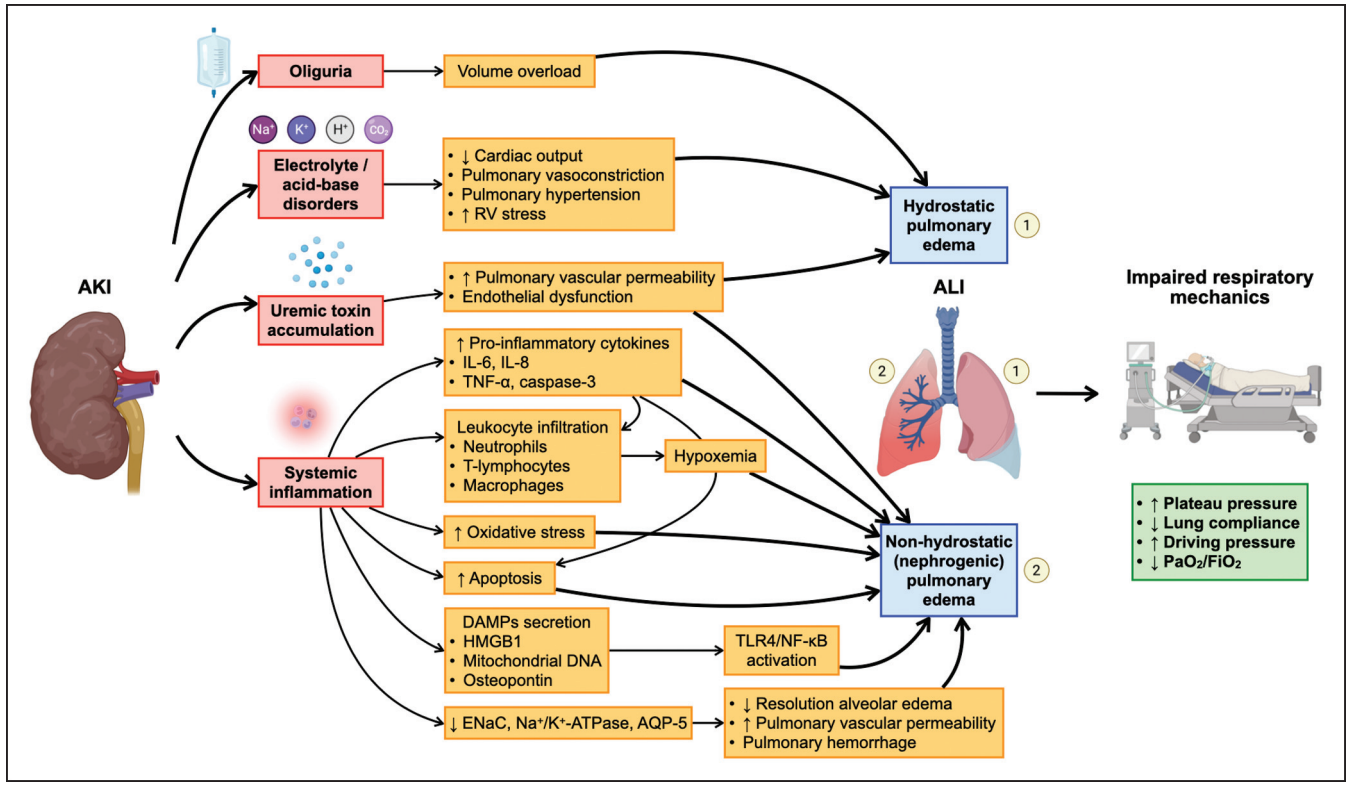

FIGURE 2. Acute kidney injury and respiratory mechanics. Acute kidney injury can initiate and perpetuate lung injury through multiple pathways, including the accumulation of uremic toxins, fluid overload, acid-base disorders, and systemic inflammatory responses. AKI, acute kidney injury; ALI, acute lung injury; AQP-5, aquaporin-5; DAMPs, damage-associated molecular patterns; DNA, deoxyribonucleic acid; ENaC, epithelial sodium channel; FiO_2, fraction of inspired oxygen; HMGB1, high-mobility group box 1; IL, interleukin; Na^+/K^+-ATPase, sodium/potassium adenosine triphosphatase; NF-κB, nuclear factor-κB; PaO_2, partial pressure of oxygen in arterial blood; RTEC, renal tubular epithelial cell; RV, right ventricular; TLR4, toll-like receptor 4; TNF-α, tumor necrosis factor-α.

may precipitate hypotension and delay resolution of AKI [58].

IMPACT OF LUNG-PROTECTIVE VENTILATION

LPV is a cornerstone strategy for patients with ARDS to minimize VILI and improve outcomes (Table 1). Emerging evidence suggests that LPV may also provide benefits by reducing the risk of AKI [59] (Table 2).

Low TV ventilation

The ARMA trial demonstrated that low TV (6 ml/kg) increased ventilator- and AKI-free days, and shortened ICU stay [3]. A secondary analysis comparing LPV to higher TV (10 ml/kg) in non-ARF/ARDS patients showed no significant difference in the risk of worsening AKI [60].

A potential undesired consequence of LPV is hypercapnic respiratory acidosis. This permissive hypercapnia may even confer anti-inflammatory and cytoprotective benefits [61,62]. Correction with bicarbonate therapy may theoretically worsen both arterial and intracellular pH, as bicarbonate is converted to CO_2, which diffuses intracellularly and accumulates in the lungs [63]. However, in severe cases, arterial pH may fall to hazardous levels, predisposing patients to hemodynamic instability, arrhythmias, and impaired RBF. During AKI, the kidneys cannot generate bicarbonate, and there is often no alternative to augment compensation. Notably, the BICAR-ICU trial found bicarbonate administration reduced mortality and mitigated the use for RRT among patients with AKI and severe metabolic acidosis [64].

Optimal positive end-expiratory pressure

The application of PEEP can improve oxygenation by lung recruitment, potentially reducing pulmonary artery pressure and RV afterload. It may also decrease left ventricular (LV) preload and afterload, thereby improving CO in cases of LV dysfunction [65].

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Table 1. Potential kidney-protective ventilation strategies and outcomes [39,41,61,70,73–74]

Intervention type	Study	Patient population / number of participants / trial type	Kidney-specific endpoints
Lung protective ventilation (LPV)	ARMA (2000)	ARDS Low TV RCT (n = 861)	More AKI-free days in LPV group
	ART (2017)	ARDS Recruitment maneuvers + PEEP	No data on AKI or RRT
Neuromuscular blockade (NMB) and LPV	ACURASYS (2010)	ARDS Early NMB RCT (*n* = 340)	Similar RRT use, more AKI-free days
	ROSE (2019)	ARDS Early NMB RCT (*n* = 1006)	No effect on mortality and AKI-free days by day 28
Prone ventilation	PROSEVA (2013)	ARDS Prone position Observational trial (*n* = 16)	No effect on RBF index, GFR index, filtration fraction, urine volume, fractional sodium excretion, and osmolar and free water clearances
Conservative fluid management	FACTT (2006)	ALI/ARDS RCT (*n* = 1000)	Trend towards reduced need for RRT with fluid restrictive strategy

AKI, acute kidney injury; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; GFR, glomerular filtration rate; PEEP, positive end-expiratory pressure; RBF, renal blood flow; RCT, randomized-controlled trial; RRT, renal replacement therapy; TV, tidal volume.

Nonetheless, the relationship between PEEP and AKI remains nuanced. Excessive PEEP can elevate intrathoracic pressure, contributing to systemic and renal venous congestion – collectively diminishing RBF and GFR, despite stable arterial pressure [27,66]. It also triggers neurohormonal activation, which may further exacerbate fluid retention and AKI [27].

Prone positioning

Prone positioning reduces lung stress and improves oxygenation. Although concerns have been raised about its potential to impair renal perfusion by increased intraabdominal pressure (IAP), several studies suggest minimal impact on kidney function. In a trial of patients with ARDS, prone positioning modestly increased IAP but had no adverse effects on RBF, GFR, urine volume, sodium excretion, or free water clearance [67]. Furthermore, a larger trial observed a nonsignificant reduction in the receipt of RRT among those receiving prone positioning [68].

Fluid management

The FACTT trial demonstrated that a conservative fluid strategy improved oxygenation, increased ventilator-free days (VFD), and shortened ICU stay compared to a liberal fluid strategy in patients with ARF/ARDS [41]. Notably, aggressive diuresis in hemodynamically stable patients did not precipitate AKI, challenging dogma that targeted fluid restriction inevitably compromises renal perfusion [41]. Compelling data suggest that diuretic use in ICU patients with ARF/ARDS and early AKI portends lower 60-day mortality [69]. The FACTT Lite trial further confirmed that fluid restriction increased VFDs and reduced AKI [70]. Hence, pairing LPV with a conservative fluid strategy may confer synergistic benefits for both respiratory mechanics and kidney protection.

Adjunctive therapies

Some adjunctive treatments used in LPV protocols may also influence the risk of AKI. For example, neuromuscular blockade, which facilitates ventilator synchrony and low TV delivery, was associated with more AKI-free days and VFDs in the ACURASYS trial [71], although this was not confirmed in the ROSE trial [72].

Inhaled nitric oxide (iNO), a rescue therapy for severe hypoxemia, has shown limited improvement in oxygenation without survival benefits [73]. However, a systematic review found that high cumulative doses of iNO increased the risk of AKI and RRT use in ARDS patients [74,75].

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Table 2. Recommendations from ADQI for implementing kidney-protective ventilation in clinical practice [59]

Statement	Grade
Interventions or modifiable risk factors to mitigate AKI among patients with ARF/ARDS requiring IMV	
• Recommend treating patients with ARF/ARDS according to the KDIGO guidelines who are at risk of or with AKI	1C
• Suggest at least daily measurement of serum creatinine and regular monitoring of urine output in patients with severe ARF/ARDS to detect development of AKI	1B
• Recommend the implementation of adequate screening measures for early reorganization of pulmonary infections, followed by early initiation of appropriate antibiotic therapy, which is associated with lower risk of AKI	1C
• Recommend monitoring of TV and ventilation pressures and application of LPV strategies in patients receiving IMV to reduce the risk of new or worsening AKI	1C
• Recommend monitoring and treatment of mechanically ventilated patients for hypotension, venous congestion, right heart failure, and IAP, which can contribute to renal dysfunction	1B
• Suggest avoiding – if possible – specific ancillary interventions known to be associated with AKI, including fluid overload, nephrotoxin exposure, and high doses of iNO	2B
Interventions or modifiable risk factors which may mitigate respiratory dysfunction among patients with AKI	
• Recommend adherence to KDIGO guidelines for AKI management, as it may translate into improved pulmonary outcomes	1D
• Suggest conservative fluid management and selected use of diuretics or RRT in patients with AKI on IMV to improve respiratory function and decrease duration of IMV in patients with ARF/ARDS	2C
• Recommend delivery of RRT to mitigate the metabolic consequences of AKI particularly where acid-base derangement may affect ventilation	1D
Impact of RRT on lung function	
• Suggest that during RRT among patients with COPD with metabolic compensation, the correction of compensatory metabolic alkalosis should be as slow as tolerated, to avoid development of acidosis	2D
Impact of ECMO on kidney function	
• Recommend close monitoring for hemolysis and markers of coagulation and inflammation	1C
• Recommend that in patients undergoing ECMO, kidney function should be monitored routinely with at least daily serum creatinine measurements and fluid balance assessment	1C
Combinations of extracorporeal lung and renal support protective for organ function	
• Recommend initiation of CRRT should be based on absolute and relative indications for critically ill patients, given there is no evidence of benefit for combining ECMO therapy with preemptive use of CRRT	1D
• No recommendation for the use of CRRT and/or hemoadsorption with the sole intention to clear pro-/anti-inflammatory mediators during ECMO	1C

ADQI, Acute Disease Quality Initiative; AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; COPD, chronic obstructive pulmonary disease; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; IAP, intraabdominal pressure; IMV, invasive mechanical ventilation; iNO, inhaled nitric oxide; KDIGO, Kidney Disease: Improving Global Outcomes; LPV, lung-protective ventilation; RRT, renal replacement therapy; TV, tidal volume.

ROLE OF EXTRACORPOREAL SUPPORT

Extracorporeal therapies (i.e., RRT, ECMO, $ECCO_2R$) are increasingly used in the context of multiorgan dysfunction. These therapies facilitate LPV strategies and may mitigate both ARF/ARDS and IMV-associated AKI, though their use also carries a risk of complications [59] (Table 2).

Renal replacement therapy

Different RRT modalities (e.g., hemodialysis or peritoneal dialysis) have shown no significant differences on respiratory function in patients with AKI [76,77]. RRT dose-intensity may be clinically meaningful. A posthoc analysis of the ATN study found that more-intensive RRT portended longer duration of IMV, lower rates of successful extubation, and more frequent reintubation events compared to less-intensive therapy [78]. More recently, a secondary analysis of the RENAL trial reported that these adverse effects may be driven by RRT modality [79▪]. Higher-intensity continuous RRT (CRRT) did not show association with delayed extubation [79▪]. Several complications have been linked to higher RRT dose-intensity, including

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hypophosphatemia, hypokalemia, nutrient losses, and prolonged oliguria [78]. Hypophosphatemia is common during CRRT and may lower the likelihood of successful extubation [79▪]. Given the essential role of phosphate in cellular energy metabolism, depletion may impair diaphragmatic contractility and impair tissue oxygen extraction, potentially contributing to adverse outcomes [78].

Extracorporeal membrane oxygenation

ECMO may reduce IMV-associated AKI by allowing for lower ventilator pressures and improving oxygenation in patients with ARF/ARDS [80,81]. Animal studies also suggest that it may enhance RBF [82]. The EOLIA and CESAR trials reported nonsignificant lower AKI rates and reduced RRT use with venovenous (VV)-ECMO compared to standard care [83,84]. These findings suggest a potential kidney-protective role, possibly through improved oxygenation, reduced hypercapnia, and mitigation of cor pulmonale. VV-ECMO also preserves pulsatile flow, thereby avoiding the renal hypoperfusion associated with the nonpulsatile flow of venoarterial (VA)-ECMO [85].

However, ECMO may exacerbate AKI, particularly in the setting of fluid overload or inadequate perfusion at the time of cannulation. Over 70% of ECMO patients develop AKI, and 60–80% receive RRT [84,86–89]. Contributing factors include hemodynamic alterations, systemic inflammation, hemolysis and pigment nephropathy, and coagulation events [90–92]. A positive fluid balance after day 3 of ECMO portends higher mortality, while achieving a net negative balance is linked to improved outcomes [88]. Although early combination of ECMO and RRT may benefit patients with fluid overload, robust evidence supporting this remains limited [93,94].

Extracorporeal CO_2 removal

$ECCO_2R$ provides a strategy to manage hypercapnia during LPV [95–97]. When coupled with CRRT, maintaining a blood flow rate >300 ml/min to ensure adequate CO_2 clearance [98,99]. Although data are scarce regarding whether $ECCO_2R$ can directly promote resolution of AKI, reduction of CO_2 may theoretically mitigate adverse hemodynamic changes that contribute to kidney injury.

CONCLUSION

IMV can significantly affect lung-kidney interactions in a bidirectional manner. Both clinical and experimental studies have demonstrated a deleterious relationship between ARF/ARDS and AKI. Injurious IMV can incite hemodynamic alterations, neurohormonal activation, and a pro-inflammatory milieu that adversely affect kidney function. In turn, AKI can exert both inflammatory and non-inflammatory effects on lungs. Evidence suggests that LPV and conservative fluid management can attenuate the direct mechanical effects of ventilation and the systemic inflammatory response arising from IMV and ARF/ARDS. These strategies can mitigate kidney injury and reduce AKI.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

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